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INCREASED MITOCHONDRIAL OXYGEN CONSUMPTION IN THE HYPERMETABOLIC INJURED RAT

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THE RISE IN total body oxygen consumption after severe thermal injury is accompanied by an increase in visceral oxygen utilization and substrate turnover, in part to meet the metabolic demands of the wound (1). The increased heat production after injury is the consequence not of altered thermoregulatory drives, but of an elevated metabolic state (2). The extent of this increased heat production suggests that accelerated intracellular oxidative processes may be primarily functioning to produce heat rather than energy to be used for synthetic and transport reactions. To assess the cellular basis for this increased oxygen utilization, we examined the function of mitochondria isolated from the liver, the metabolically most active organ.

MATERIALS AND METHODS

Male rats (475 to 500 gm) were acclimated in a light-cycled, temperature-controlled environment and then divided into three groups: control (sham, unburned); 60% total burn surface (full-thickness burn), and partially starved. The thermally injured rat is an established model of postinjury hypermetabolism; a burn of this size results in a 30% to 40% increase

Table 1

	Group (N = 12)		
	Control	Partially starved	Burned
State 3	46.52	47.76	62.95*
RCR (State 3/State 4)	5.30	5.33	5.17
Phosphorylation rate	82.35	84.53	110.16*
Weight change (%)	+4	−11	−12

*Control vs burn, $P < 0.01$.

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in oxygen consumption (3). The partially starved rats were fed a diet sufficient to produce a weight loss similar to the loss in burned rats to which they were paired. The rats were then killed and liver mitochondria were separated by differential centrifugation. Oxygen uptake was measured polarographically with a Clark electrode. Resting oxygen uptake (state 4, presence of substrate, succinate) in nmole $O_2 \cdot min^{-1} \cdot$ mg protein^{-1}, maximum oxygen uptake (state 3, after addition of ADP), respiratory control ratio (RCR, an index of mitochondrial efficiency), and phosphorylation rates in nmole ADP $\cdot$ min$^{-1} \cdot$ mg protein^{-1} were calculated at 25, 30, and 37 C. Statistical significance was determined by ANOVA: SD were within 15% of means.

RESULTS

Mitochondrial oxygen utilization increased significantly (+35%) in the injured rats, with a parallel increase in phosphorylation of ADP to ATP (see Table 1). RCRs in all three groups were identical (no uncoupling). Increasing temperature accelerated oxygen uptake rates in mitochondria from both control (46.5, 63.5, and 78.0 at 25, 30, and 37 C, respectively) and injured rats (63.0, 79.4, and 96.22), but the temperature dependence of reaction rates (Q_{10} effect) was identical in each treatment group.

DISCUSSION

The increase in total body oxygen consumption of the injured rats was associated with a similar increase at the cellular level. These changes could not be explained by weight loss and were not influenced by high temperatures, both of which characterize the burned patient. Oxidation was not uncoupled from phosphorylation, and the elevated heat production in such patients cannot be explained by diversion of energy into futile biochemical pathways. This augmented energy-efficient oxygen uptake and energy production in mitochondria partially explains the increased total body oxygen consumption associated with postinjury hypermetabolism.

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